

ABSTRACTS

This section of the JOURNAL is published in collaboration with the two abstracting Journals, ABSTRACTS OF WORLD MEDICINE and OPHTHALMIC LITERATURE, published by the British Medical Association. The abstracts are divided into the following sections: Syphilis (Clinical, Therapy, Serology, Pathology, Experimental), Gonorrhoea, Non-Gonococcal Urethritis and Allied Conditions, Chemotherapy, Public Health and Social Aspects, Miscellaneous. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. All subsections will not necessarily be represented in each issue.

SYPHILIS (Clinical)

Bacterial Endocarditis superimposed on Syphilitic Aortitis. (Endocarditis bacteriana desarrollada sobre aortitis sifilítica.) ACEVES, S., ELIZALDE R. A. and GONZALEZ LUNA M. *Arch. Inst. Cardiol. Méx.*, **27**, 231 (1957) 10 figs, bibl.

The authors have made a detailed study of the records, together with available sections and specimens, of 1,815 necropsies carried out between September, 1944, and February, 1956, at the National Institute of Cardiology of Mexico. There was cardiovascular disease in 1,785 cases, syphilitic mesaortitis being present in 142 (8.5 per cent.) of these and bacterial endocarditis in 104 (5.8 per cent.). Of the 142 cases of syphilitic aortitis, 26 (18.3 per cent.) were in women, compared with 27 (25 per cent.) of the 104 cases of bacterial endocarditis.

In 100 of the 142 cases of syphilitic aortitis the aortic valves were involved, and in nine cases in this group (and in none of the others) bacterial endocarditis was superimposed on the syphilitic disease. These cases were all in males whose ages varied from 28 to 55 years, with an average of 39 years; two of them had additional evidence of rheumatic involvement of the mitral valve. Out of 476 cases of rheumatic disease of the aortic valve in this series, bacterial endocarditis was superimposed in 45 (9.4 per cent.); thus the incidence of bacterial endocarditis in aortic valvular disease due to syphilis was virtually identical with that found in rheumatic aortic valvular disease.

Details are given of the clinical findings in the nine cases of bacterial endocarditis superimposed on syphilitic disease. In three cases there was no fever, in three it was atypical and irregular, and in three it was very occasional; in four cases there was clubbing of the fingers, while in an equal number the spleen was palpable. Urinary changes were present in six cases, but the finding of Osler nodes was not recorded in any. Heart failure had a rapid and progressive course and did not respond to treatment. There was clinical evidence in two cases of embolism in the limbs and in two of myocardial infarction. Purpura was noted in one case only. Serological tests for syphilis gave positive results in six cases and negative in two, and were not performed in one. Blood culture was positive in only two out of the six cases in which it was carried out. Pulmonary infarction, right-sided or bilateral, occurred

in eight cases. In five there was electrocardiographic evidence of coronary insufficiency, and of the seven cases in which there was no rheumatic involvement of the mitral valve, six had left bundle-branch block.

The incidence of both bacterial endocarditis and syphilitic aortitis in Mexico is declining. In a 2-year period ending in 1946 among 310 necropsies at the Institute there were 28 cases of bacterial endocarditis and 44 of syphilitic aortitis, whereas in a similar period ending in 1956 among 371 necropsies there were only eleven cases of bacterial endocarditis and twenty of syphilitic aortitis.

[This is a detailed and valuable study.] *Eric Dunlop*

Neurosyphilis in the Bantu Male. WOODS J. D. (1957). *S. Afr. Lab. clin. Med.*, **3**, 326, 12 refs.

Syphilis is one of the commonest diseases amongst the Bantus. Neurosyphilis, at the King Edward VIII Hospital in Durban, was about 0.5 per cent. of all (5,000) cases and 9.5 per cent. of all neurological cases seen during 1950. They comprised: G.P.I. (one), tabes (four), gummatous meningitis (eight), meningomyelitis (seven), spinal cord gumma (one), optic atrophy (three). One case with gummatous meningitis had a bilateral papillitis with complete blindness in the right eye, and a visual acuity of 6/24 in the left eye. Intensive treatment with penicillin brought about symptomatic cure in 2 months. On discharge visual acuity was 6/12 in the right, and 6/5 in the left eye. The criteria for diagnosis were very strict and probably the incidence was higher. Amongst the other neurological cases were five of optic atrophy, with negative serological tests but abnormal spinal fluids. They had been inadequately treated with arsenicals.

A. Jokl

Interstitial Heredo-Syphilitic Keratitis and Trauma. (Kératite interstitielle hérédo-syphilitique et traumatique.) VOISIN J. and POULIQUEN Y. (1957). *Bull. Soc. ophtal. Fr.*, Nos. 7-8, 415.

Argyll Robertson Symptom in Diabetes Mellitus. A Contribution to the Neuropathy of Ocular Diabetes. (Sintomo di Argyll-Robertson in corso di diabete mellito. (Contributo alla conoscenza delle neuropatie oculari diabetiche.)) MOSCI L. (1957). *Ann Ottal.*, **83**, 269. 9 refs.

Asymmetry of Fingerlength—a Symptom of Congenital Syphilis? (Fingerlängenasymmetrie—Symptom der angeborenen Syphilis?) RÖSLER HANS-DIETER (1958). *Arch. klin. exp. Derm.*, **205**, 526. 1 fig., 9 refs.

Problems in the Clinical Diagnosis of Neurosyphilis. (Problemen in de klinische diagnostiek van lues nervosa.) DIERCKX A. L. (1957). *Folia psychiat. neerl.*, **60**, 405–417. 1 fig.

Psychosis of General Paresis. A Case of Study and Discussion. CLAMAN L. (1957). *J. nerv. ment. Dis.*, **125**, 57. 6 refs.

Significance of Minimal Symptoms in the Central Nervous System in Cases of Late Syphilis. (O znaczeniu mikrosymptomów ze strony układu nerwowego u chorych z kila późna). BARCIKOWSKA-STEMPIEŃ A., HORSKI-HORONCZYK S., and PRUSIŃSKI A. (1957). *Neurol. Neurochir. Psychiat. pol.*, **7**, 933. 5 refs.

SYPHILIS (Therapy)

Cortisone and Syphilis. Results of Corticotherapy Preceding Penicillin Treatment in 120 Cases of Syphilis. (Cortisone et syphilis. Résultats de la corticothérapie précédant la cure pénicillinée dans cent vingt cas de syphilis.) GRACIANSKY P. DE, and GRUPPER C. (1957). *Rev. franc. Et. clin. biol.*, **2**, 579. 5 figs, 30 refs.

The authors present a further report of their experiences at the Hôpital Saint-Louis, Paris, with preliminary cortisone followed by penicillin in the treatment over a 5-year period of 120 patients with syphilis at various stages. Various schedules and dosages of cortisone were employed, including 100 mg. cortisone by mouth or intramuscular injection for periods ranging from one to 5 days or longer. Hydrocortisone was also used, and in two cases an intravenous infusion of 25 mg. ACTH (corticotrophin) in glucose-saline was given. Local treatment with cortisone was employed in cases of interstitial keratitis and hydrocortisone was instilled into the joints in cases of arthropathy associated with tabes dorsalis. During the last year of the study thirty cases were treated with 30 mg. daily of Δ -1-dehydrocortisone ("cortancyl") for 6 days, a single injection of long-acting penicillin being given on the 4th and 5th days. Throughout this investigation the authors have consistently given either a single injection or a single course of injections of various types of long-acting penicillin. During the last 2 years of the study a single injection of 2,400,000 units of a long-acting preparation was the sole penicillin therapy administered. All the patients were admitted to hospital during the treatment period and the usual examinations and tests carried out.

One of the authors' many interesting conclusions is that cortisone prevents or attenuates the Herxheimer reaction either in its clinical form or as a febrile response in all stages of syphilitic infection. It modifies the clinical manifestations of all stages of the disease, this modification being usually towards amelioration and healing of the lesions, but complete healing was not observed

with cortisone alone. The findings in respect of primary lesions differed from those of Turner and Hollander (*Bull. Johns Hopk. Hosp.*, 1950, **87**, 505) who studied the effect of cortisone on artificially induced syphilis in rabbits. Favourable results were obtained in the treatment of a small number of cases of neuro-syphilis with lightning pains which had proved resistant to other forms of therapy. Further, signs of activity of the syphilitic infection were modified by cortisone therapy, treponemes often disappearing from primary and secondary lesions, and the titre of reagin in the serum in cases of primary and secondary syphilis was reduced or the usual rapid increase in titre in these cases was halted. In cases of tertiary syphilis with clinical evidence of activity there was also some fall in the reagin titre, but in cases of latent syphilis with a low titre no fall was observed after cortisone therapy. In the few cases in which the treponemal immobilization test was performed a fall in the titre of the immobilizing antibody was observed following cortisone. Changes in the cerebrospinal fluid were reversed, the raised cell and protein contents first returning to normal, followed later by the serological and colloidal gold reactions.

Cortisone did not appear to modify the sensitivity of *Treponema pallidum* to penicillin, and it was of particular value in hypersensitive subjects and those with a history of previous penicillin sensitivity. It was also found useful in the treatment of pregnant women and in patients with syphilis of the cardiovascular and central nervous systems.

R. D. Catterall

Experiences in Penicillin Treatment of Endemic Syphilis in Serbia. (In English. ILIC, S. (1957). *Dermatologica (Basel)*, **155**, 287. 5 figs.

After the war of 1939–45 a systematic campaign for the control of endemic syphilis was undertaken in Serbia, previous attempts at such control having been only partially successful. Two treatment regimens were employed:

- (1) procaine penicillin in oil with 2 per cent. aluminium monostearate (P.A.M.)
- (2) penicillin with bismuth.

Serological tests were carried out in established laboratories to ensure reliable standards of work; this was an important factor because a high proportion (80 per cent.) of the patients whose blood was tested had latent infections.

The results obtained with penicillin and bismuth were not significantly different from those obtained with P.A.M. alone, but, as the author points out, the dose of bismuth was too small to exert a curative effect or to inhibit the action of penicillin. The results achieved with 6 mega units penicillin were better than those obtained with doses of 3·6 or 4·2 mega units. The author comments on the surprisingly high percentage of seronegative results after treatment; 18 months after the start of penicillin therapy the percentages of seronegative results in two districts where the disease had recently been endemic were 63 and 71 respectively; in three other districts where syphilis had been present for a long time

the percentages were 38, 38, and 60 respectively. In control tests carried out after more than 42 months the figures were either unchanged or better. *Robert Lees*

Results of Oral Penicillin Therapy in Congenital Syphilis.

(Ergebnisse der oralen Penicillin-Behandlung bei Lues connata.) CAILLOUP H. and WELLER, R. (1957) *Msehr. Kinderheilk.*, **105**, 321. 1 fig., 20 refs.

The authors describe, from the University Paediatric Clinic, Munich, the results of treatment of congenital syphilis in newborn infants with 100,000 units of oral benzylpenicillin in saline per kg. body weight daily, divided into six or eight doses per day over a period of 14 days. Usually only one course was given, but in severe cases admitted to hospital more than 4 weeks after birth a second course lasting 10 to 14 days was given 2 or 3 weeks later. The only untoward effect noted was "deterioration of faeces" in 14 per cent of cases, but one child died of severe "dyspepsia". In two cases the motions improved when parenteral administration of penicillin was substituted for oral. About one-third of the cases showed a Herxheimer reaction in the form of pyrexial spikes up to 38.5° to 40°C. which lasted 12 to 24 hours, and two cases which were initially sero-negative became transitorily sero-positive on the 16th and 18th days respectively.

Of 95 infants, with definite radiological or serological signs of syphilis, two died on the day following admission, another after 6 weeks' tetany, and the infant with severe dyspepsia on the 11th day of treatment; in a fifth fatal case death was due to intercurrent infection after removal from hospital against medical advice. In two-thirds of the cases there was hepato- and splenomegaly, and in 40 per cent. anaemia; 30 per cent. showed skin lesions, and bone changes were present in 43 of the 95 children, mostly in those with clinical and serological findings indicating severe infection. The authors point out that bony changes in sero-negative children are not reliable criteria of active infection, since they may represent a healing stage as the result of transplacental transmission of penicillin from the mother treated during the last two trimesters of pregnancy. Under treatment the skin lesions disappeared in 6 to 8 days, anaemia (treated by blood transfusion in severe cases) in 2 to 3 weeks, and in twenty of the children with bone lesions these were no longer present on re-examination after one year. Conversion of the serological finding in babies treated within 3 weeks of birth occurred within 60 days; when treatment was begun later conversion did not occur before 3 to 4 months.

At follow-up examination, after periods ranging from 5 years in thirty cases to less than one year in sixteen cases, no abnormal signs were detected except "saddle nose" in several cases and some degree of frontal bossing; one child suffered from microcephaly and mental retardation, but this was possibly due to birth trauma. *F. Hillman*

Results of Treatment of Neurosyphilis with Very High Doses of Penicillin in Combination with Fever compared with those with Standard Penicillin Therapy Alone.

(Ergebnisse der Behandlung van Neurosyphilis mit sehr hohen Penicillindosen in Kombination mit Fieber im Vergleich zur üblichen alleinigen Penicillinbehandlung.) DEGWITZ, R. (1957). *Nervenarzt*, **28**, 371.

From observations made during the years 1951 to 1954 at the City and University Neurological Clinic, Frankfurt am Main, during which time cases of neurosyphilis were treated with penicillin alone in a course totalling 10 mega units, it was found that the many resistant cases responded better to a combination of penicillin and fever therapy. The author now reports the results in 56 cases of active neurosyphilis which were treated with high doses of penicillin—1.2 mega units daily to a total of 30 mega units—and, as soon as their clinical state permitted, with artificial fever therapy in addition. The patients were observed for periods up to 2 years and from this follow-up study the following three main points emerged:

- (1) only 10 per cent. of the cases showed continuing disease activity in the cerebrospinal fluid (C.S.F.) after 4 months, compared with 20 per cent. of cases treated with penicillin therapy alone.
- (2) only three of the 56 patients relapsed, compared with 7 out of 34 given routine therapy;
- (3) the trend toward sero-negativity developed more rapidly and the improvement in the C.S.F. cell counts, which began within a few days of institution of therapy, was sustained in most cases, the C.S.F. being cleared within 4 months.

As the author points out, such a therapeutic regimen is of importance in Germany where, in contrast to some other countries, there has been a persistently high incidence of neurosyphilis, largely due to the often inadequate treatment of patients with primary and secondary syphilis after the last war. *Allene Scott*

Problems of the Tests of Cure of Syphilis. (Zur Problematik unserer Kriterien der Syphilisheilung.) LANGER, E. and KRÜGER, H. (1957). *Z. Haut- u. Geschl.-Kr.*, **23**, 310, 18 refs.

Treatment of Primary Syphilis with Synnematin B. WHEELER, A. H., JAMES, K., LEA, W., and CURTIS, A. C. (1957). *A.M.A. Arch. Derm.*, **76**, 735. 4 refs.

Single Session Therapy of Early Syphilis. RAJAM, R. V., RANGIAH, P. N., SNOWMINI, C. N., and IYENGAR, M. C. R. (1957). *J. Indian med. Ass.*, **29**, 467. 2 refs.

SYPHILIS (Serology)

Behaviour of Serum Protein Lability Reactions and Electrophoretic Findings during the Specific Treatment of Syphilis. (Das Verhalten von Serumweißstabilitätsproben und Elektrophorese während der spezifischen Behandlung der Lues.) WOLF, G. (1957). *Arch. klin. exp. Derm.*, **204**, 566.

At the Miners' Hospital, Stollberg, Germany, 91 patients with syphilis, in most cases in the latent stage, were investigated by a battery of serum protein tests

which the author names "protein lability tests", these including the Takata-Ara reaction, the Weltmann coagulation test, the Gross flocculation test, and the formol-gel, thymol turbidity, water turbidity, and cadmium sulphate tests. In addition, paper electrophoresis of the serum proteins was performed. The patients had no history of liver disease.

The protein lability tests, which were carried out both before and after 177 courses of penicillin treatment, were abnormal before treatment in 10.7 per cent and after treatment in 10.1 per cent. [It is not stated what proportion of patients showed these changes both before and after treatment.]

The electrophoretic pattern was initially abnormal in 14 per cent. of cases, the most consistent change being an increase in the gamma-globulin fraction. It was noted that during treatment the electrophoretic pattern sometimes resembled that seen in acute infections, but after treatment it tended to become normal. Specific tests for parenchymatous liver damage were carried out in some cases, but these gave only normal results. It is considered that the abnormalities found in the serum were due to increased activity of the reticulo-endothelial system rather than to damage of the liver parenchyma.

[It is difficult to assess the value of this paper since many of the laboratory findings are not given in detail and no statistical evaluation of the significance of the results is attempted.]

G. W. Csonka

Sensitivity and Specificity of Reiter Protein Complement-Fixation (RPCF) Test for Syphilis. REIN, C. R., KELCEC, L. C., D'ALESSANDRO, G., and DE BRUIJN, J. H. (1957). *J. invest. Derm.*, **28**, 459. 8 refs.

Protein extracted from the Reiter treponeme by cryolysis and precipitation with ammonium sulphate (D'Alessandro's technique) has been used by the authors at the University Hospital, New York, as an antigen in complement-fixation tests for syphilis. It was used at titres of 1 in 80 in the one-fifth-volume Kolmer method and of 1 in 250 in the Kent technique. Comparative tests showed that the latter was the more reproducible and eliminated many anticomplementary results, while its sensitivity was comparable to that of the Kolmer test.

Sera were then tested in parallel with four tests using lipoidal antigens (the Mazzini, V.D.R.L., Rein-Bossak, and a cardiolipin complement-fixation test) and four tests using treponemal antigens (the treponemal immobilization and immune adherence tests, the complement-fixation test of Portnoy and Magnuson, and the Reiter protein complement-fixation test (R.P.C.F.T.)). Examination of sera from 94 patients with treated early syphilis showed that the sensitivity of the R.P.C.F.T. was comparable to that of the other treponemal tests, while it was more sensitive than any of the tests using lipoidal antigens—the most sensitive of these, the V.D.R.L. test, gave 43 positive or weakly positive reactions compared with 61 with the R.P.C.F.T. In tests on sera from 112 patients with treated late or latent syphilis the sensitivity level of the R.P.C.F.T. was also found to be similar to that of the other treponemal tests. An indication of the

specificity of the R.P.C.F.T. was obtained from tests on sera from 99 patients who were thought to be biological false positive reactors fifteen of whom had lupus erythematosus. None of the treponemal tests gave positive reactions with any of these 99 sera. A. E. Wilkinson

Comparison of Several Serologic Tests for Syphilis using *Treponema pallidum* Antigen with Sera from Selected Diagnostic-problem Patients. FALCONE, V. H., and HARRIS, A. (1957). *Amer. J. clin. Path.*, **28**, 91. 19 refs.

A comparative investigation is reported from the Venereal Disease Research Laboratory of the U.S. Public Health Service, Chamblee, Georgia, in which a number of different serological procedures using virulent *Treponema pallidum* as the antigen were employed in the testing of 28 syphilitic sera and 200 sera suspected of giving biological false positive reactions in the standard tests for syphilis. These procedures were:

- (1) Treponemal immobilization (T.P.I.) test (three different methods);
- (2) *T. pallidum* methylene blue (T.P.M.B.) test (affinity of virulent treponemes for methylene blue being lost when they are incubated in the presence of syphilitic serum and complement);
- (3) *T. pallidum* complement-fixation (T.P.C.F.) test;
- (4) *T. pallidum* immune adherence (T.P.I.A.) test;
- (5) *T. pallidum* agglutination (T.P.A.) test with unabsorbed and absorbed sera.

Of the 28 syphilitic sera, six or seven were non-reactive to the T.P.I. test by each of the three methods used, seven were non-reactive to the T.P.M.B. test, nine to the T.P.C.F. test, twelve to the T.P.I.A. test, and six and fourteen to the T.P.A. test with unabsorbed and absorbed sera respectively. Of the 200 sera suspected of giving biological false positive reactions, 48 to 71 were reactive to the T.P.I. test by the three different methods, 71 to the T.P.M.B. test, 56 to the T.P.C.F. test, 75 to the T.P.I.A. test, and 91 and 18 to the T.P.A. test with unabsorbed and absorbed sera respectively.

The authors conclude that "it seems likely that a premise of absolute specificity for a testing procedure may not be tenable, even though it is based on the fact that the antigen is prepared from the casual agent of the disease".

R. R. Willcox

Treponemal Immobilizing Antibodies in Syphilis. II. Technique and Interpretation of the Treponemal Immobilization Test. (Les anticorps immobilisants des tréponèmes dans la syphilis. II. Technique et interprétation du test d'immobilisation des tréponèmes.) FRIBOURG-BLANC, A. *Ann. Derm. Syph. (Paris)*, **84**, 410.

A full description is given of the author's method of carrying out the treponemal immobilization (T.P.I.) test [for details of which the original paper should be consulted]. The main differences from Nelson's original technique are that the medium is modified by increasing the thioglycollate concentration to 0.125 g. per 100 ml. and by introducing magnesium (0.1 g. MgSO₄ per 100

ml.), and sodium glycerophosphate (0.075 g. per 100 ml.). These changes are said to improve the survival of the treponemes. It is stated that metal Seitz filters should not be used for sterilizing the medium as traces of metals absorbed during filtration may adversely affect the treponemes. The complement dose is increased, 0.15 ml. active complement being used in the "test" tubes and 0.1 ml. inactivated complement in the "control" tubes. [The reason for using different volumes in the two tubes is not stated.] Quantitative tests on two positive control sera are included in each batch of tests, human sera being preferred to rabbit sera for these because of the anticomplementary properties of the latter. The incubation period has been extended from 18 hrs to 21 to 23 hrs at 35°C. as this permits good survival of the treponemes and allows the reaction to proceed almost to completion.

In the assessment of qualitative tests the author considers that sera giving up to 15 per cent. specific immobilization should be regarded as negative and those giving 15 to 95 per cent. as weakly positive, these results being usually found very early or very late in the infection. The importance of confirming these weakly positive results by examination of a second specimen of serum is stressed. The finding of 100 per cent. specific immobilization is thought to indicate persistence of treponemal infection.

As syphilis progresses, the level of immobilizing antibody in the serum rises rapidly and soon produces 100 per cent. specific immobilization. Once this level has been reached a quantitative test is essential for assessment of the amount of antibody present, the titre being expressed as the highest dilution of serum which will immobilize 50 per cent. of the treponemes under the test conditions. Such titres may vary from 50 to as much as 3,000. In untreated cases with latent infection titres of 150 to 500 are commonly found. After treatment there may be a fall in titre followed by stabilization at a lower level; reversal to negativity probably only occurs if treatment is given very early in latency. Very high titres—1,000 to 3,000—are often found in patients with actively progressive tertiary lesions. In contrast, titres of 8 to 20 may possibly reflect only residual antibodies left after healing. Under satisfactory conditions the reproducibility of the quantitative test should be within 30 to 40 per cent., so that too much significance cannot be attached to small variations in titre.

A. E. Wilkinson

Problem of Doubtful Results in the Nelson-Mayer Test:

Technical Precautions in Their Interpretation. (Il problema dei risultati dubbi del test di Nelson-Mayer: accorgimenti tecnici per la loro interpretazione.) BONCINELLI, U., VACCARI, R., and PINCELLI, L. (1957). *G. ital. Derm.*, **98**, 217. 16 refs.

The authors writing from the University of Modena, point out that treponemal immobilization in the Nelson-Mayer (T.P.I.) test depends in the last instance on the amount of immobilizing antibody present. Between the non-reacting, non-syphilitic sera and the clearly reacting syphilitic sera there often occur a small number of doubtful sera producing 20 to 50 per cent. immobilization, and these results are not easily reproducible. Apart

from "undesired" variables in the test, the only other variable is the amount of immobilizin in the serum. When the antibody content and specific immobilization of a large number of sera are plotted an S-shaped curve is obtained of which the vertical part corresponds to the doubtful zone of 50 per cent. immobilization. In the examination of some 3,000 samples of serum the authors found that 2.64 per cent. gave a doubtful result.

Occasionally an injection of killed Reiter's treponemes raises the patient's antibody level so that a subsequent T.P.I. test gives a positive result. But this biological approach is time-consuming and the authors therefore carried out two parallel series of T.P.I. tests in doubtful cases, in one of which they used a double amount of serum without doubling the other reagents in the test; this showed that the doubled amount of serum by itself had no undue immobilizing activity. Thus of 505 sera examined, 331 gave a negative result in both tests (less than 20 per cent. immobilization), 151 a positive result in both (51 to 100 per cent. immobilization), and 23 gave doubtful or different results in the two tests. Of these 23 sera nine were doubtful in the regular test but became positive when double amounts of serum were used, immobilization rising from an average of 32.2 to 70.6 per cent. With five sera the result remained doubtful (30 to 37 per cent. immobilization) even when the double quantity of serum was used, and these were therefore considered to be non-specific. The remaining nine sera gave 13 to 19 per cent. immobilization in the regular test; with the double amount of serum, three became clearly positive and six moved into the doubtful zone. In view of the clinical background and the doubling of the immobilization titres, all these sera were considered to be specifically positive. The technique is therefore of most use in the case of doubtful sera, and the simultaneous execution of the two series of tests has the advantage of eliminating the possibility of biological changes occurring in the sera and reagents between tests.

F. Hillman

The Pallida Reaction. Its Significance in the Modern Serology of Syphilis. (Die Pallida-Reaktion. Ihre Bedeutung für die moderne Lues-Serologie.) RUGE, H., KNOTHE, H., and OTTEN, O. (1957). *Dtsch. med. Wschr.*, **82**, 1231. 14 refs.

The author first briefly traces the history of treponemal antigens. One of the most recently introduced, the "pallida" antigen, is obtained by ultrasonic disintegration of Reiter's treponeme. From reports in the literature it appears that this antigen binds the protein antibody of syphilitic sera, and in the author's view it is therefore more specific than the lipid antigens, including cardiolipin. Reiter's treponeme is, however, not suitable for the Nelson-Mayer treponemal immobilization test. Evidence is quoted from the literature to show that the pallida antigen provides a useful additional test, and when read in conjunction with the results of other tests using treponemal antigens it equals the treponemal immobilization test in efficiency and gives fewer false positive reactions.

At the University Institute of Hygiene, Kiel, some 1,000 sera were tested with the pallida antigen, the Wassermann reaction using cardiolipin and a traditional antigen, the Meinicke II reaction, and the cardiolipin micro test (C.M.T.). The results are presented in a table. The pallida antigen gave only two (0.3 per cent.) false positive results and at the same time 568 (80.3 per cent.) specific positive results. None of the other tests gave a lower percentage of false positive reactions, only the C.M.T. gave a higher number of true positive reactions; at the same time, however, this last test gave also sixteen (2.2 per cent.) biological false positive results. With numerous syphilitic sera the pallida antigen was the only one to give a consistently positive result. Compared with the C.M.T. the pallida reaction gives a titre which is 2.5 times higher. The authors suggest that the drawback of high cost of this antigen is counterbalanced by the usefulness of the reaction.

F. Hillman

Use of Passive Haemagglutination in the Diagnosis of Syphilis. (Aportaciones al empleo de la hemaglutinación pasiva en el diagnóstico de la sífilis.) GALLEGO CAPILLA, J. (1957). *Rev. Sanid. Hig. públ. (Madr.)*, **31**, 249. Biblio.

The sensitization of erythrocytes with antigens, antigenic fractions, and haptens is being used more and more frequently for the investigation of specific antibodies. Sensitized erythrocytes agglutinate when placed in contact with specific antibodies, this phenomenon being the reaction of passive haemagglutination. In his work at the Provincial Institute of Hygiene, Granada, the author has applied this reaction to the diagnosis of syphilis, using Meinicke (M.K.R. II), Sachs Witebsky S.W. II, cardiolipin (V.D.R.L.), and Reiter treponeme antigens. The technique followed was a modification of that of Escobar (*Laboratorio*, 1954, **17**, 115), who used Kahn antigen; full details of the author's method are given. Good results were obtained when M.K.R. II and S.W. II antigens were used. However, all attempts with cardiolipin antigen and with Reiter antigens from whole and disrupted treponemes failed owing to the development of haemolysis during sensitization. The literature is extensively reviewed.

Eric Dunlop

Rapid Plasma Reagin Test for Syphilis. PORTNOY, J., GARSON, W., and SMITH, C. A. (1957). *Publ. Hlth. Rep. (Wash.)*, **72**, 761. 12 refs.

A review of the literature on the use of plasma in serological tests for syphilis shows that Burdon, in 1930, first observed that plasma gave more sensitive results in the Kahn and Kline tests than did serum. This was confirmed subsequently by other workers, who noted that reliable results were obtained with unheated plasma suspended in choline chloride. The present authors describe a rapid plasma reagin (R.P.R.) test in which they use V.D.R.L. antigen emulsion resuspended in 10 per cent. choline chloride in normal saline. One drop of the antigen is mixed with three drops of plasma, obtained by centrifuging blood collected with any anticoagulant. The mixture is then rotated on a concave slide and clumping is observed microscopically over a period of 4 minutes.

A comparison of the results obtained with this test and the results of the standard V.D.R.L. slide test (a total of 1,609 tests were performed) showed that the R.P.R. was consistently more reactive than the V.D.R.L. In no instance was there a negative response with the R.P.R. test and a positive reaction with the V.D.R.L. It is suggested that the greater reactivity noted was due to a higher reagin content in plasma, together with an enhancing effect due to choline. Discrepancies between the results of the two tests were encountered only in old cases of treated syphilis. Not only does the new test cost very little more than the V.D.R.L. test to perform, but there is a great saving in time and personnel. In a series of 47,579 screening tests the R.P.R. method was used with apparently satisfactory results. Allene Scott

Contributions to the Immunobiological Diagnosis of Neurosyphilis. I. Agglutinating Antibodies in the Cerebrospinal Fluid. (Beiträge zur immunbiologischen Diagnostik der Nuerolues. I. Agglutinierende Antikörper im Liquor cerebrospinalis.) HIPPIUS, H. KUNZ, I., and WENDE, S. (1957). *Artzl. Wschr.*, **12**, 1051. 18 refs.

From the Psychiatric and Neurological Clinic of the Free University of Berlin the authors report the application of a treponemal agglutination reaction to 859 specimens of cerebrospinal fluid (C.S.F.), 59 of which were obtained from patients with neurosyphilis and 796 from patients without neurosyphilis, while in four cases a firm diagnosis was not possible. The agglutination reaction used was that described by Roemer and Schlipköter (*Dtsch. med. Wschr.*, 1953, **78**, 345; *Z. Hyg. Infekt.-Kr.*, 1955, **140**, 528) and the antigen used was a formalin-conserved suspension of Reiter's treponeme. Briefly, the technique consists in mixing 0.4 ml. C.S.F. with 2 drops of the antigen. After energetic shaking the tubes are incubated at 37°C. for 3 hours and then kept until the next day at room temperature. Control tubes are made up with normal saline in place of C.S.F. Quantitative reactions were not performed, but a number of serological tests, including both complement-fixation and flocculation reactions, were carried out for comparison.

Of the 59 specimens from patients with neurosyphilis, agglutinating antibodies were demonstrated in 33 (56 per cent.), the reaction being negative in 26 (44 per cent.). With fifteen (1.8 per cent.) of the 796 specimens from non-syphilitic patients "non-specific" positive reactions were obtained. [The authors use the term biological false positive reaction in an unorthodox way throughout the text.]

It is concluded that the specificity and sensitivity of the treponemal agglutination reaction with C.S.F. are not such as to permit of its use alone in the diagnosis of neurosyphilis. However, it is suggested that it has a place alongside other, already established, serological tests.

R. D. Catterall

Treponemal Antigens in the Diagnosis of Syphilis. (Les antigènes tréponémiques dans le diagnostic de la syphilis.) BENAZET, F., PEILLARD, M. M., BROTTES, H., LARTIGAU, G., and LAYOUS, A. (1957). *Rev. Hyg. Méd. soc.*, **5**, 515. 6 figs, bibl.

This report from the Desgenettes Military Hospital, Lyons, evaluates the results of complement-fixation tests for syphilis performed with either a suspension of the Reiter treponeme (Pallignost) or a protein extract of this treponeme as antigen; in both cases the Kolmer technique was used. Reactions with the protein antigen were incubated in the cold, but this was found to give an unduly high proportion of positive results with the Pallignost antigen; this difficulty could be overcome by incubation, limited to one hour, at 37°C. instead of in the cold. It was noted that zone reactions were common with the protein antigen. A number of the usual tests for syphilis were also performed, a total of 1,969 sera from patients whose clinical status was known being examined, not all of them, however, by the whole range of tests. Cases were classified as "syphilitic" if the treponemal immobilization (T.P.I.) reaction was positive or had previously been positive, if there were indubitable clinical signs or a history of syphilis, or, in latent cases, if the standard tests for syphilis (S.T.S.) repeatedly gave a positive result.

The test using the Pallignost antigen was found to be more sensitive than either the S.T.S. or the T.P.I. test with sera which were classified as syphilitic, but that using the protein extract as antigen was considerably less sensitive than any of the other types of test in these cases. The authors [rightly] point out the fallacy of comparing the sensitivity of tests which detect different antibodies.

In specificity the tests with the treponemal antigens compared favourably with the S.T.S. The test with Pallignost antigen gave non-specific reactions in 3 per cent. of tests on 997 non-syphilitic sera, the test with protein-extract antigen in 0.6 per cent. of 751 sera, while the S.T.S. gave non-specific results in 11.6 per cent. of 1,447 sera tested, an alarmingly high figure; these were mainly results of the Kahn test. The majority of non-specific results with the treponemal antigens were found in sera from patients with conditions known to be associated with transient false positive reactions, although some were found in apparently healthy individuals.

For diagnostic purposes the authors recommend the combined use of a complement-fixation test and a flocculation test, using cardiolipin antigens together with a complement-fixation test using the treponemal-suspension antigen. When the two types of test are in agreement there is, in their opinion, little chance of error; when the tests give discrepant results recourse should be had to the T.P.I. test. They consider, however, that not enough is yet known about the behaviour of the test with treponemal suspension in treated cases for it to be used as a guide to the adequacy of treatment.

A. E. Wilkinson

Use of Soluble Treponemal Protein Antigen in a Haemagglutination Reaction. (Impiego dell'antigene treponemico proteico solubile (ATPS) in una reazione di emoagglutinazione.) LAMEDICA, G., and ROBERT, L. (1957). *Igiene mod.*, 50, 345. 16 refs.

Of the four antigens isolated from Reiter's treponeme, the soluble protein antigen is the most specific, the

corresponding antibody appearing in the blood soon after the primary infection and reaching its maximum titre during the secondary stage. From the Institute of Hygiene of the University of Genoa the authors describe an haemagglutination reaction in which this antigen, adsorbed on to tanned sheep erythrocytes, is used. The specificity of such a reaction was demonstrated by repeated absorption of serum from a rabbit sensitized with soluble protein antigen and by a haemagglutination-inhibition test.

A total of 274 sera from treated cases of syphilis were subjected to the Kolmer complement-deviation test with cardiolipin antigen, the V.D.R.L. micro-flocculation test with cardiolipin antigen, the Kolmer test with soluble protein antigen, and the authors' haemagglutination test. The results fell into four groups:

- (1) Negative results were obtained with 207 sera in the first three tests, but seventeen (8.24 per cent.) of the 207 gave positive haemagglutination, often only at the highest dilution of serum. The presence of an incomplete antibody in the lower dilutions of serum might well have accounted for this phenomenon, but a Coombs test on the cells in these dilutions gave an inconclusive result. The presence of an agglutination-inhibiting factor in the serum which became ineffective in high dilution is another possible explanation, but most probably the reaction was non-specific.
- (2) Of nineteen sera giving a positive reaction to the Kolmer-cardiolipin and V.D.R.L. tests, but a negative reaction to the Kolmer test with soluble protein antigen, three gave a positive haemagglutination reaction; there were all from long-treated cases of syphilis.
- (3) Of 34 sera giving a positive reaction to the first three tests, five gave a negative haemagglutination reaction—probably because the haemagglutination test is less sensitive than the complement-fixation techniques.
- (4) Of fourteen sera giving a negative reaction to the two tests with cardiolipin and a positive reaction to the Kolmer test with soluble protein antigen, three gave a negative haemagglutination reaction.

The results in these four groups were subjected to variance analysis and the differences found to be statistically significant. In 28 cases—about 10 per cent. of the total—the results of the standard and haemagglutination tests disagreed. The authors argue that the series was very small, and that possibly more highly purified antigens may give fewer false positive agglutination reactions. Work is in progress which, they hope, will define more sharply the limits of the technique outlined here.

F. Hillman

Albumins and Syphilitic Reagins in the Aqueous Humour.

(Les albumines et les réagines syphilitiques de l'humeur aqueuse.) ALAERTS, L. (1957). *Docum. ophthalm.*, 11, 143.

The protein rate in the aqueous humour varies with the general condition, e.g., fevers, cancerous tumours, syphilis, and allergy.

Syphilitic reactors in the aqueous humour can be detected by Chediak's micro-reaction: they show up soon after the appearance of the syphilitic condition and remain throughout the second and third stage.

(Author's Summary)

Composition of Cardiolipin. RICE, F. A. H. (1958). *Science*, **127**, 339. 9 refs.

Present Situation in Regard to the Serologic Tests for Syphilis. KNOLLE, K. C. (1957). *Tex. Rep. Biol. Med.*, **15**, 904. 11 refs.

Some Aspects of the Treponemal Immobilization Reaction in Cases of General Paralysis under Treatment. (Alguns aspectos da reacção de imobilização treponêmica nos paráliticos gerais em tratamento.) FONSECA, A. DA, and RAMOS, S. (1957). *Trab. Soc. port. Derm.*, **15**, 151. 7 refs.

New Method of Saving Time and Material in the Preparation of the Basal Medium for the Nelson-Mayer Test. (Neue zeit- und materialsparende Möglichkeiten bei der Herstellung des Basalmediums für den Nelson-Mayer Test). FUCHS, G. H. P. and AHRENS, C. B. F. W. (1958). *Schweiz. Z. allg. Path. Bakt.*, **21**, 74. 11 refs.

Kahn and *Treponema Pallidum* Complement-Fixation Results in Syphilis and False Positive Factors. GUYON, J. F., and COLE, C. C. (1957). *J. Mich. med. Soc.*, **56**, 1579.

SYPHILIS (Experimental)

Experimental Syphilis in White Mice. (Die experimentelle Syphilis der weissen Maus). BERLINGHOFF, W., (1957). *Derm. Wschr.*, **136**, 929. 1 fig., 5 refs.

In experiments which were carried out at the Friedrich Schiller University, Jena, white mice were inoculated with the Nichols strain of *Treponema pallidum* by the intramuscular and intraperitoneal routes. The mice remained asymptomatic; but when they were exsanguinated 2 months after inoculation and their tissues inoculated into rabbits syphilitic lesions were produced after the usual interval. Blood from the mice gave negative results with the treponemal immobilization test, but the blood of the rabbits gave a positive result. It is suggested that the fact that mice experimentally inoculated with *T. pallidum* do not suffer from chronic asymptomatic syphilis may be because the treponemes live in symbiosis with the mice, or because some form of natural immunity protects these animals without weakening the virulence of the treponemes.

G. W. Csonka

Role of Temperature in the General Dissemination of Syphilis. (Le rôle de la température dans la généralisation de la syphilis expérimentale). LONGHIN, S. POPESCO, A., and VOLOSCEANU, D. (1957). *Arch. roum. Path. exp. Microbiol.*, **16**, 293. 16 figs, 18 refs.

Natural Immunity of the Rabbit Foetus to *Treponema pallidum*. (Immunité naturelle du foetus de lapin vis-à-vis de "*treponema pallidum*"). PAUTRIZEL, R., MAYER, G., RIVASSEAU-COUTANT, A., and SZERSNOVICZ, F. (1957). *Rev. Immunol. (Paris)*, **21**, 383. 2 figs, 34 refs.

GONORRHOEA

Sensitivity of Gonococci to Penicillin and its Relationship to "Penicillin Failures". THAYER, J. D., FIELD, F. W., MAGNUSON, H. J., and GARSON, W. (1957). *Antibiot. and Chemother.*, **7**, 306. 1 fig., 3 refs.

When the marked sensitivity and apparent lack of development of resistance of the gonococcus to penicillin was first realized it was thought by some that the incidence of gonorrhoea throughout the world would show a sharp decline. In an attempt to ascertain why this has not been so the sensitivity and bacteriostatic response to penicillin of 31 strains of gonococci obtained from female patients were intensively studied at the Venereal Disease Experimental Laboratory of the U.S. Public Health Service, University of North Carolina. Of these patients eleven were treated with 1·8 mega units penicillin aluminium monostearate (P.A.M.) which resulted in bacteriological cure, but in ten out of the twenty patients given 600,000 units of P.A.M. the treatment was bacteriologically a failure.

All the strains initially isolated showed *in vitro* a relatively high sensitivity to penicillin (range of concentrations 0·005 to 0·2 unit per ml.), including those strains from the ten patients in whom treatment failed. In order to determine whether the action of penicillin was bactericidal or bacteriostatic penicillinase was added to all the assay tubes in a concentration sufficient to destroy the penicillin, the tubes being then incubated for a further 48 hrs. For seventeen out of nineteen strains so tested penicillin was bacteriostatic for the gonococcus when penicillinase inactivation was applied after 24 hrs' exposure to penicillin, whereas if the exposure was allowed to continue for 48 hrs the action of the antibiotic was bactericidal. As the authors remark, however, these observations of the relatively high sensitivity of all the strains of gonococcus to penicillin and the bacteriostatic action of penicillin after 24 hrs' exposure fail to account for the therapeutic relapses.

G. W. Csonka

Failure of Penicillin to kill Phagocytosed *Neisseria gonorrhoea* in Tissue Culture. THAYER, J. D., PERRY, M. I., MAGNUSON, H. J., and GARSON, W. (1957). *Antibiot. and Chemother.*, **7**, 311. 6 refs.

In a further study carried out at the Venereal Disease Experimental Laboratory, University of North Carolina, tissue cultures of HeLa cells were used to determine whether phagocytosed gonococci are protected from the bactericidal action of penicillin. With the strain of *Neisseria gonorrhoea* investigated studies *in vitro* showed that 24 hrs' exposure to the action of penicillin was sometimes bacteriostatic, whereas exposure for 48 hours was invariably bactericidal. Thus 48 hrs' exposure of the infected monolayer of HeLa cells ensured that all extracellular gonococci would be dead and that any outgrowth of

the cocci after this period must be the result of protection by the HeLa cells. The death of extracellular gonococci being thus assured, the penicillin was then inactivated by penicillinase, when it was found that outgrowth of the gonococcus from the HeLa cells occurred after 72 to 96 hrs, whereas in the absence of protecting tissue cells in the control media the action of penicillin was bactericidal. There is no proof yet of phagocytosis by fixed tissue cells occurring in the human host, but, as is pointed out, such an occurrence would be a potential source of re-infection.

G. W. Csonka

Credé's Prophylaxis in Ophthalmia Neonatorum. (Über die Credé'sche Prophylaxe Neugeborenenblennorrhoe.) SALVISBERG, H., and SCHÖNENBERG, F., (1957). *Ophthalmologica (Basel)*, 134, Suppl. p. 48. 109 refs.

Since Credé introduced 2 per cent. silver nitrate instillation immediately after birth in 1880, the incidence of ophthalmia neonatorum has fallen drastically. Silver nitrate is still used in some places but in others less irritating silver preparations are used such as silver acetate 1 or 2 per cent. (which is the obligatory prophylactic in Austria) or the colloidal silver preparations. The latter, however, are not without danger of contamination and panophthalmitis following colloidal silver drops after cataract extraction has been described. Recently, sulphonamides and penicillin were tried with satisfactory results but with both of these allergic reactions and development of bacterial resistance may occur. With penicillin, the watery solution loses potency rapidly and fresh solutions have to be prepared. In oily or ointment form it keeps longer. A questionnaire was sent to 34 European hospitals and clinics on modern prophylaxis and the incidence of gonococcal ophthalmia and the replies have been tabulated. The results of investigations with Desogen (Geigy), a quarternary ammonium compound, are given, and it is concluded that in 0.5 per cent. solution it is suitable for instillation as a prophylactic agent against ophthalmia neonatorum.

M. Klein

Study on the Growth Requirements of *Neisseria gonorrhoeae* and its Clinical Application. GRIFFIN, P. J., and RIEDER, S. V. (1957). *Yale. J. Biol. Med.*, 29, 613 22 refs.

Gonorrhoea in the Female. PARKER, M. S. (1958). *Neb. St. med. J.*, 43, 58. 4 refs.

Acute Gonorrhoea treated by Combined Penicillin-Streptomycin Injections. MIKHAILOV, A. N. (1957). *Sovetsk. Med.*, 21, 37. 4 refs.

NON-GONOCOCCAL URETHRITIS AND ALLIED CONDITIONS

Acute Hemorrhagic Cystitis. An Infection associated with Pleuropneumonia-like Organisms and related to Urethritis and Prostatitis. BERG, R. L., WEINBERGER, H., and DIENES, L. (1957). *Amer. J. Med.*, 22, 848. 1 fig., 26 refs.

A controlled investigation carried out at the Massachusetts General Hospital, Boston, and the U.S. Naval Hospital, Chelsea, Massachusetts, showed that acute haemorrhagic cystitis (a term the authors prefer to acute abacterial pyuria) is an infective venereal condition of the urethra, prostate, bladder, and sometimes of the kidneys, due to pleuropneumonia-like organisms (PPLO) which are sensitive to streptomycin and the tetracyclines but insensitive to penicillin and the sulphonamides. PPLO tended to disappear with remission of the disease, whether spontaneous or therapeutic, and were present in some patients without urinary symptoms. They were far more often found in unexplained urinary infections, and were isolated in all fifteen cases presenting a typical picture of abacterial pyuria. The authors state that, although PPLO are commonly cultured from the vulva, they have not observed any cases of cystitis due to these organisms in women. In acute haemorrhagic cystitis, there are general disturbances, pyrexia, and leucocytosis, together with conjunctivitis and dermatitis, as in Reiter's disease.

W. Skyrme Rees

Tetracycline Hydrochloride in the Treatment of Non-Gonococcal Urethritis. WILLCOX, R. R. (1958). *J. roy. Army med. Cps.*, 104, 44. 1 ref.

Non-Gonorrhoeal Inflammatory Diseases of the Urethra in Males. PORUDEMINSKI, I. M. (1957). *Sovetsk. Med.*, 21, 27. 16 refs.

CHEMOTHERAPY

Penicillinase in the Treatment of Penicillin Reactions. MINNO, A. M., and DAVIS, G. M. (1957). *J. Amer. med. Ass.*, 165, 222. 2 refs.

Untoward reactions to penicillin are variously estimated to occur in 0.1 to 5 per cent. of those receiving the drug, and there is no known way of predicting which reactions will clear promptly and which will be so severe as to tax all known therapeutic resources. In this paper from the U.S. Naval Hospital, Great Lakes, Illinois, the authors report the results of giving penicillinase—which has been reported to reduce the level of circulating penicillin in the blood to zero within an hour—to 32 patients suffering from severe reactions to either benzathine or procaine penicillin, which usually took the form of urticaria with generalized pruritus, severe arthralgia, or a serum-sickness-like reaction. The usual dose was 1,000,000 units penicillinase intramuscularly (but the injection was given intravenously to two patients, of whom one responded satisfactorily but the other developed a severe rigor and slight cyanosis). Penicillinase was the sole agent of treatment in twelve of the cases, the others receiving antihistaminics as well, but no other medication.

Of the 32 patients, fifteen became ambulatory and asymptomatic within 24 hrs and 5 within 48 hrs. In the remaining twelve cases the signs and symptoms abated, but it was 4 to 6 days before all had disappeared. Pruritus was promptly relieved in nearly every case. In eleven cases a second injection was given after 48 hrs. No toxic manifestations were encountered, but there was pain and

tenderness at the site of the intramuscular injection for 24 hrs. The necessity to use steroids has not arisen since the introduction of penicillinase. Antihistaminics and penicillinase seem to be complementary and their combined use has appeared to reduce morbidity. An addendum to the paper contains a brief report of ten additional cases, in eight of which the patient recovered completely in 48 hrs and in one in 72 hrs; the remaining patient required admission to hospital for 5 days.

A. Ackroyd

Fatal Reactions to Penicillin. Evaluation of a Test for Sensitivity. SMITH, V. M. (1957). *New Engl. J. Med.*, **257**, 447 4 figs, 4 refs.

A simplified method of detecting penicillin sensitivity was given a clinical trial at a U.S. Army Hospital at Augsburg, Germany. The method consisted in the application of a solution of procaine penicillin (300,000 units per ml.) to a forearm skin scratch and the conjunctival sac, the response being considered positive if an area of skin erythema over 1 cm. in diameter, a skin weal, and conjunctival watering, redness, and oedema developed within 15 minutes. Of the 1,365 subjects tested, 25 gave a positive response, and ten of these are known to have had an anaphylactic reaction to penicillin, which in one case proved fatal. A generalized sensitivity reaction to the test in one case subsided after injection of adrenaline subcutaneously. In seven additional subjects who were known to have had recent acute anaphylactic reactions to penicillin the results of the skin and conjunctival tests were positive although all were receiving antihistamine therapy at the time. In several subjects the reaction to the skin test was positive and that to the eye test was negative, while in others the reverse was the case; the author therefore recommends that both tests should be performed simultaneously. Intramuscular injections of penicillin were given to a group of 778 patients who had shown a negative response to the sensitivity tests; only one had a mild anaphylactic reaction a few minutes afterwards.

The author concludes that by carrying out these tests, which are safe, simple, reliable, and specific, potentially fatal immediate anaphylactic responses to penicillin may be avoided.

Gerald Sandler

Antibiotic Combinations. Tetracycline, Erythromycin, Oleandomycin, and Spiramycin, and Combinations of Tetracycline with Each of the Other Three Agents—Comparisons of Activity *in vitro* and Antibacterial Action of Blood after Oral Administration. JONES, W. F., and FINLAND, M. (1957). *New Engl. J. Med.*, **257**, 481 and 536. 14 figs, bibl.

The authors writing from the Thorndike Memorial Laboratory and City Hospital (Harvard Medical School), Boston, review the literature on the combined use of certain related antibiotics. They are critical [justifiably] of some of the methods used and of the interpretation of data concerning synergism or antagonism of antibiotic combinations. They concur in the findings of Garrod (*Brit. med. J.*, 1957, **2**, 57; *Abstr. Wld Med.*, 1957, **22**,

427), who, contrary to the claims of other workers, failed to demonstrate synergism in certain combinations.

They then report studies of the activity of certain antibiotic combinations. First, the respective activities *in vitro* of oleandomycin and spiramycin were compared with that of erythromycin against pathogenic strains of various Gram-positive cocci. Erythromycin was found to be the most effective and spiramycin the least effective of the three. A comparison was then made of the activity *in vitro* of these three antibiotics and tetracycline each used alone, and of combinations of the last-named with each of the others. It was found that none of the mixtures, in any of the proportions used, possessed superior antibacterial activity when compared with that of the more active component of the corresponding mixture. Finally, the antibacterial action of the blood of healthy subjects was assayed after ingestion of each of the four antibiotics singly and of combinations of tetracycline with each of the three erythromycin-type antibiotics. The findings were similar to those obtained in the tests carried out *in vitro*.

The authors conclude that oleandomycin and spiramycin are sufficiently inferior to erythromycin to indicate that their general use in the treatment of infections is unwarranted, and that administration of the antibiotic combinations discussed in this paper is to be discouraged.

E. G. Rees

Antibiotic Combinations. Antistreptococcal and Antistaphylococcal Activity of Normal Subjects after Ingestion of Erythromycin or Chloramphenicol or Both. JONES, W. F., and FINLAND, M. (1957). *New Engl. J. Med.*, **257**, 744. 4 figs, 15 refs.

Controlled studies were made on the antistreptococcal and antistaphylococcal activity of the plasma of six normal subjects after ingestion of single doses of either 500 mg. or 1,000 mg. erythromycin or chloramphenicol, or equal amounts of both these agents. Erythromycin yielded the greatest activity, and chloramphenicol the lowest, and the mixture gave intermediate values. The activity obtained from the larger dose was higher, in each test, than that derived from smaller doses of the corresponding agent.

[Authors' summary]

Studies on Synergism with Twelve Antibiotics against Thirty Hospital Strains of *Staphylococcus aureus*. ELLIOTT, H. J., and HALL, W. H. (1957). *J. Lab. clin. Med.*, **50**, 242. 1 fig., 9 refs.

In this study the authors have analysed the activity of twelve antibiotics, both singly and in 66 paired combinations, against thirty strains of *Staphylococcus aureus* isolated at the Veterans Administration Hospital, Minneapolis, during 1954. A bacterial inoculum of 0.4 ml. of a 1:100 dilution of each strain in an 18 hr. broth culture was mixed with doubling dilutions of each antibiotic. The bacteriostatic end-point was taken as the lowest concentration of antibiotic that prevented visible growth after 18 hrs at 37°C. All clear tubes were subcultured on nutrient agar plates, and the lowest antibiotic concentration that prevented growth on subculture was

recorded as the bactericidal end-point. An antibiotic concentration of 6.25 units or μg . per ml. was arbitrarily chosen to distinguish susceptible from resistant strains—that is, organisms were considered to be susceptible if there was no growth and resistant if there was growth at the concentration. The agar-diffusion method and replica plating were used to demonstrate synergism, antagonism, or additive effects of combinations of antibiotics.

It was shown that a high degree of resistance to penicillin, streptomycin, and the tetracyclines was frequent. Cross-resistance between these antibiotics was common, and was practically uniform among the individual tetracyclines. Resistance was rare to the newer antibiotics which were not available in 1954 when these staphylococci were originally isolated. The combined activity of any two antibiotics was not usually enhanced if the strain of staphylococcus was highly resistant to one or both separately; thus synergism was infrequent between penicillin, streptomycin, and the tetracyclines. On the other hand potentiation of both bacteriostatic and bactericidal activity occurred with pairs of the newer antibiotics to which the hospital strains were most susceptible; this activity was usually additive rather than synergistic. The most effective combinations were novobiocin with vancomycin, bacitracin with chloramphenicol, and erythromycin with cycloserine.

D. Geraint James

PUBLIC HEALTH AND SOCIAL ASPECTS

Syphilis Control in Upstate New York. THOMAS, E. W. (1957). *N. Y. St. J. Med.*, **57**, 3639. 2 figs.

Status of Venereal Disease Control in Texas. DOANE, A. R. (1957). *Tex. Rep. Biol. Med.*, **15**, 842.

MISCELLANEOUS

Chemotherapy in Bubonic Lymphogranuloma Venereum. A Clinical and Serological Evaluation. GREAVES, A. B., HILLEMANN, M. R., TAGGART, S. R., BANKHEAD, A. B., and FELD, M. (1957). *Bull. Wld Hlth. Org.*, **16**, 277. 5 figs, 18 refs.

The effectiveness of chemotherapy in bubonic lymphogranuloma venereum has been studied in 43 cases seen

at the Polk Health Clinics, Washington, D.C., the drugs used being chloramphenicol, aureomycin, oxytetracycline, and sulphadiazine. These were given to 26 patients; the remaining seventeen patients received symptomatic treatment only and served as controls. The diagnosis was established by complement-fixation test, and syphilis and chancroid were excluded: in all but five cases the Frei test was positive. The progress of the bubo, the development of other lymphopathies, and the titre of the complement-fixation test were used to assess the course of the disease. The dose of each antibiotic was 1 g. initially followed by 0.5 g. four times daily for 14 days; the dose of sulphadiazine 2 g. initially followed by 1 g. four times daily for 10 to 28 days.

From the results it appeared that the clinical response to chemotherapy, as measured by the duration of the bubo after treatment was started, was not greatly superior to the response to symptomatic therapy alone. Serological evaluation, however, showed a distinct benefit in the drug-treated series; the antibody level declined much more rapidly, and by the end of a year's observation almost half the patients gave a negative result. According to the authors this may be assumed to indicate a diminution in the amount of virus present or its elimination from the body.

It is concluded that specific chemotherapy should be given as a routine in cases of lymphogranuloma venereum, and since there is no evidence of the superiority of antibiotics over sulphadiazine the latter should be the drug of choice.

[This is a valuable study of the chemotherapy of bubonic lymphogranuloma venereum with an adequate control group, though the variable clinical course of the disease makes assessment difficult.] *Robert Lees*

Recent Changes in Venereal Diseases. LANIGAN-O'KEEFE, F. M. (1957). *Irish J. med. Sci.*, 230 No. 377.

Comparative Study of Japanese and American Antigens for the Detection of Dermal Sensitivity in Chancroid [In English] BOAK, R. A. (1957). *Jap. J. exp. Med.*, **27**, 155. 7 refs.

Short History of Yaws in Trinidad. FAWKES, M. A. (1957). *W. Indian med. J.*, **6**, 189. 3 figs., 7 refs.